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(54) Title: CONTACT LENSES WITH POLYMER BOUND ASEPTICIZING AGENTS

(57) Abstract

Contact lenses having asepticizing agents bound to the lens polymer and methods for preparation of the same.

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CONTACT LENSES WITH POLYMER BOUND ASEPTICIZING AGENTS

Cross Reference to Related Applications

This is a continuation-in-part of my application Serial No. 797,295, filed May 16, 1977, entitled SYMMETRIC HYDROGEL MATRIX FOR CONTACT LENSES, which discloses aseptic contact lens polymers, and of my application Serial No. 920,670, filed June 30, 1978, entitled STYRENE COPOLYMERS FOR CONTACT LENSES which discloses lens polymers asepticized by copolymerization of hydroxy substituted benzene monomers.

Background of the Invention

It has long been known that the human eye harbors potentially pathogenic microorganisms.[3,4,5,6,7] Soft contact lenses are particularly subject to attack.[7] The need for careful handling of contact lenses generally, and regular sterilization of soft contact lenses has presented a long-standing problem in the art.[2-9] Serious and intensive efforts have been made to solve this problem. The most extensive effort has related to a lens identified as the ASEPTOPLAST (trademark) lens.[3-6] Germicidal agents, hexachlorophene and a commercial germicide, COROBEX CP-4 (trademark) consisting of 0.3% boric acid, 2.25% phenylmercuric borate, 0.11% 2-ethyl-hexanol, and 0.75% di-isobutyl phenoxyethoxy-ethyl dimethyl ammonium benzyl chloride, balance inactive, were blended into the monomer before polymerization of the lens polymer, thus effectively forming a polymer with the germicide in solid solution in the polymer matrix form the ASEPTOPLAST lenses. These lenses were studied extensively and establish the biostatic effect of germicidal agents dissolved in solid lens

polymers. (The term "biostatic" is a term of art and is used here in the same sense as used by Wesley.[4])

The ASEPTOPLAST lens approach, although a significant effort to solve a very serious and long-standing problem, is limited by the very serious risk that leaching of the asepticizing agents from the lens polymer will not only decrease the biostatic action of the lens but, more importantly, may irritate or seriously damage the eye of the user.

These long-standing and very difficult problems of prior art lenses generally, and of prior art soft lenses in particular, are overcome according to the present invention by providing a biostatic lens polymer in which the asepticizing agent is permanently bound to the polymer. The lens material itself is resistant to microbiological action and tends to prevent or inhibit growth of pathogenic organisms in the user's eye.

The polymers which are suitable for preparation of contact lenses as modified according to this invention are known lens polymers, and the monomer and polymer systems and methods of handling these systems are prior art. Many examples of lens polymers and monomers used for polymerization and copolymerization to produce lens polymers are described herein and in the references cited at the end of this specification, which are incorporated herein as fully as though set forth for disclosure of the monomers, polymers and copolymers and processing methods disclosed therein.

Disclosure of the Invention

Asepticizing agents inherently containing or modified by reaction to include a reactive group capable of polymerization, e.g., groups referred

to here as a "polymerizable vinyl" group, i.e., one which is polymerized with lens monomers also including a polymerizable vinyl group to bond the aseptic agent to the backbone of the polymer. In an alternative embodiment, an asepticizing agent is bonded to the polymer by reaction of a reactive group on the asepticizing agent with a reactive group on the already polymerized polymer.

In my copending application Serial No. 797,295, filed May 16, 1977, I disclosed the reaction of benzyl-trialkyl ammonium halide, e.g., benzyl trimethyl ammonium chloride, bound to a lens polymer backbone by copolymerizing p-vinyl-benzyl trimethyl ammonium chloride with both hard lens polymers and soft lens polymers, e.g., methyl methacrylate and ethylene glycol dimethacrylates and soft lenses, e.g., hydroxyethyl methacrylate and triethylene glycol dimethacrylate polymers, as well as many modifications of these basic polymer systems. Other polymer systems disclosed included methyl methacrylate-vinyl pyrrolidone-triethyleneglycol dimethacrylate polymers, alpha-methyl-styrene modified methyl methacrylate polymer lenses, methacrylic acid modified methyl methacrylate lenses and vinyl triphenyl silane lenses. The general applicability of the principal of copolymerizing a polymerizable vinyl group containing asepticizing agent with polymerizable vinyl group containing lens polymers generally is, thus, disclosed in my aforesaid application Serial No. 797,295.

Specific examples of asepticizing agents which can be applied within this broad inventive concept, namely hydroxyl substituted benzene compounds, e.g., phenols, resorcinols and catechols, are more specifically disclosed in my aforesaid co-pending application Serial No. 920,670, filed June 30, 1978.

Additional examples of the inventive concept as applied to a variety of polymers and a variety of asepticizing agents are disclosed herein.

Broadly, the invention contemplates contact lens polymers generally, without respect to the particular polymer or copolymer matrix, to which asepticizing agents are chemically bonded, without respect to the nature of the particular asepticizing agent. A preferred form of the invention contemplates bonding polymerizable vinyl group containing asepticizing agents into the backbone of polymers and copolymers formed by polymerizing polymerizable vinyl group containing lens monomers. Another preferred form of the invention contemplates the bonding, through any pair of reactive groups, of an asepticizing group to an already formed polymer. Specific preferred examples and embodiments of the invention are set forth in detail in the following specification.

Best Mode for Carrying Out the Invention

The present invention contemplates alternative routes to forming lens polymers and lenses in which the asepticizing agent is bonded to the polymer. Depending upon the nature of the asepticizing agent and the polymer, one particular approach may, in different circumstances, be preferred.

Bonding Through a Polymerizable Vinyl Group

Monomers for polymerization or copolymerization of contact lens polymers by the polymerization of polymerizable vinyl groups are very well known and generally, are suitable for use in this invention. The principles of this invention are most valuably utilized in connection with hydrogel lenses. Hydrogels, and their application to lenses have been disclosed by Wichterle et al, along with many variations of this

class of materials, in a series of patents issuing over the past nearly two decades.[33,38,42-43,46-47,50-51,55-56,61,64] Suitable hydrogel polymer systems include the polymerization products of polyethylene glycol methacrylate and polyethylene glycol dimethacrylates; triethylene glycol methacrylate, methyl methacrylate and triethylene glycol dimethacrylate; dimethyl amino ethyl methacrylate and triethanol amine dimethacrylate.[33] Also applicable are hydrogels formed by the polymerization of esters of acrylic and methacrylic acid with alcohols having hydrophilic groups which after polymerization impart hydrophilic properties to the polymer. Wichterle et al disclose a number of acrylic and methacrylic acids, alcohols and cross-linking agents suitable for use in preparing hydrogels of this class.[38]

Starting materials for producing these hydrogels include the esters of acrylic and methacrylic acid with alcohols having hydrophilic groups which after polymerization impart hydrophilic properties to the polymer obtained. A major portion of a monoester of acrylic or methacrylic acid with a bifunctional alcohol which has an esterifiable hydroxyl group and at least one additional hydrophilic functional group is co-polymerized with a small amount of a diester of these acids and of an alcohol which has at least two esterifiable hydroxyl groups until a shape retaining body is obtained.

The polyfunctional alcohols forming one of the constituent elements of the aforementioned monoester, and preferably also the alcohol constituent of the diester may have additional hydrophilic groups in their molecule which make the esters water soluble even after two or more of the hydroxyl groups are esterified by

the acrylic or methacrylic acid.

Many derivatives of acrylic or methacrylic acid other than the esters mentioned are also suitable as monomers in the copolymerization reaction leading to these hydrogels. These include, but are not limited to the following monomers:

Dimethylaminoethyl methacrylate, piperidinoethyl methacrylate, morpholinoethyl methacrylate, methacryllyglycolic acid, methacrylic acid as such, the monomethacrylates of glycol, glycerol, and of other polyhydric alcohols, the monomethacrylates of dialkylene glycols and polyalkylene glycols. The corresponding acrylates may be substituted for the methacrylates.

Similarly, the diesters mentioned above may be replaced by other cross-linking agents such as triethanolamine dimethacrylate, triethanolamine trimethacrylate, tartaric acid dimethacrylate, triethylene glycol dimethacrylate, the dimethacrylate of bis-hydroxyethylacetamide.

This general class of polymers has been used to prepare substantially anhydrous sparingly cross-linked hydrophilic polymers capable of being swollen when placed in water which consists of a high percentage, e.g., 98% or more, of a monoester of acrylic or methacrylic acid and an alcohol having an esterifiable hydroxyl group and at least one additional hydroxyl group and less than 2% of a cross-linking agent of a diester of the alcohol.[56]

Hydrogel lens polymers having selected properties and advantages which are suitable for use in this invention have been developed by a number of workers. Seiderman[48] discloses one such formulation.

These polymers result from polymerization of hydroxyalkyl acrylate and methacrylate esters in copolymeric composition with minor amounts of a longer chain alkyl acrylate or methacrylate ester comonomer and a cross-linking comonomer such as allyl diglycol carbonate, glycol diacrylates, glycol dimethacrylates, polyglycol diacrylates and dimethacrylates, allyl methacrylates, triallyl cyanurate, divinylbenzene, and trivinylcyclohexane.

Examples of suitable hydroxyalkyl methacrylates are: 2-hydroxyethyl methacrylates, 2-hydroxypropyl methacrylate, and the like. Other hydroxyalkyl methacrylates can be used with varying degrees of satisfaction. Also, alkylamino alkyl methacrylates, such as 2-dimethylaminoethyl methacrylate, 2-butylaminoethyl methacrylate, dimethylaminopropyl methacrylamide, quaternary salts of the same and the like, can be used.

Examples of suitable alkyl methacrylates are: methyl methacrylate, ethyl methacrylate, propyl methacrylate, butyl methacrylate and the like.

Examples of suitable longer chain alkyl methacrylates are: lauryl methacrylate, or other alkyl methacrylates wherein the alkyl radical thereof contains from out 5 to about 20 carbon atoms in the alkyl chain, such as capryl, palmityl, stearyl, cyclohexyl methacrylates, and alkyl cyclohexyl, and cyclo-octyl and cyclo-dodecyl methacrylates.

Examples of suitable cross-linking agents are: olefin glycol dimethacrylates such as: ethylene glycol dimethacrylate, diethylene glycol dimethacrylates, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, polyethylene glycol dimethacrylate, 1, 4-butylene glycol dimethacrylate and 1,3-butylene glycol dimethacrylate.

Examples of suitable catalysts are: benzoyl peroxide, chlorobenzoyl peroxide, lauryl peroxide, tertiary butyl peroxycarbonate, isopropyl peroctoate, etc.

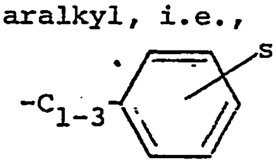
Modified polyvinylpyrrolidone resins in which a mixture of polyvinyl pyrrolidone, vinyl pyrrolidone, a hydroxyalkyl methacrylate and a cross-linking agent are reacted[53] may also be reacted with polymerizable vinyl group containing asepticizing agents according to the principals of this invention. Polymerizable vinyl group containing aseptic agents may, according to this invention, be polymerically bonded into hydrogels modified by the inclusion of glycidyl methacrylate, glycidyl acrylate and glycidyl crotonate[60], hard plastic hydrogels including triethylene glycol dimethacrylate[65] soft hydrophilic lenses modified by the inclusion of trimethylolpropane trimethacrylate,[66] hydrogel copolymers of dihydroxyl alkyl acrylates and methacrylates copolymerized with alkyl acrylates and methacrylates,[72] soft contact lenses made of a copolymer derived from a monomer mixture of hydroxyethyl or hydroxypropyl acrylates and methacrylates with 4 to 13 carbon hydroxyalkyl acrylates and methacrylates,[75] soft lenses prepared from copolymers modified by the inclusion of polyalkylene glycol acrylates and methacrylates,[76] hydrophilic polymers from polymerization of diester-free glycol monoester of acrylic or methacrylic acid and polyalkylene oxide acrylate or methacrylate.[80] It is within this invention to polymerize aseptic agents which include a polymerizable vinyl group with styrene modified acrylate and methacrylate polymers as disclosed in my co-pending application Serial No. 920,670, with vinyl pyrrolidone modified hydroxy alkyl acrylate hydrogels, with alkyl ether acrylates and methacrylates with vinyl silane and with substituted alkyl and hydroxyalkyl acrylate and

methacrylate monomers, all as disclosed in my copending application Serial No. 979,295, with methyl methacrylate modified hydroxy ethyl methacrylate lenses as disclosed in my copending application Serial No. 930,665 with the known acrylic and methacrylic lens polymers and modifications of acrylic and methacrylic lens polymers.

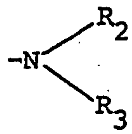
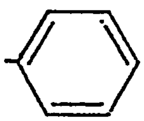
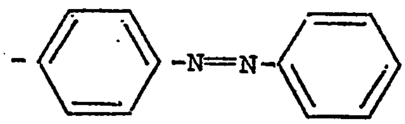
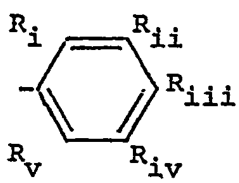
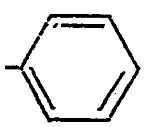
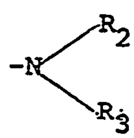
It is also within the contemplation of this invention to polymerically bond a polymerizable vinyl group containing aseptic agent into the backbone of vinyl lens polymers of all classes. As used here, vinyl lens polymers include any polymer or copolymer resulting from the polymerization of reactive vinyl groups. Vinyl compounds which may be used, as either major or minor constituents, in lens polymers of the class with which this invention may be used include the following compounds which include a polymerizable vinyl group having the general structure:

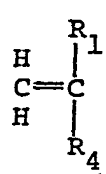
$$\begin{matrix} H & H \\ C{=}\!\!\!\!& C{-}R_1, \\ H & \end{matrix}$$

and homalogous allyl and crotyl compounds, wherein R_1 is selected from a group consisting of: (1) -Cl; (2) -F; (3) -Br; (4) lower, 1-4 carbon, alkyl, halogen, amine and hydroxy substituted lower alkyl; (5) lower, 1-4 carbon, alkoxy, halogen, amine and hydroxy substituted alkoxy; (6) lower, 6-9 carbon, aralkyl and phenyl substituted aralkyl, i.e.,



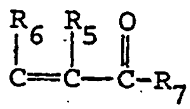
wherein s is -H or a single or double substituent, alike or different, on the phenyl ring, said substituent being selected from the group consisting of -Cl, -F, -OH, $-NH_2$, $-NO_2$, $-SO_4$, $-CH_3$ and $-OCH_3$;

(7)  , wherein R_2 and R_3 are selected from the group consisting of -H, lower alkyl, 6-9 carbon aralkyl,  ; (8)  ; (9) -CN; (10)  , wherein one or more of R_i through R_v is selected from the group consisting of -OH, -Cl, -F, lower alkyl, lower alkoxy, $-NO_2$, $-SO_4$,  , and  , R_2 and R_3 being as defined above; R_1 always being selected to permit polymerization or copolymerization of the vinyl group monomer, vinylidene monomers,

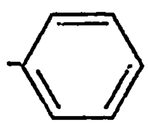


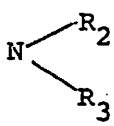
wherein R_1 and R_4 are as defined with respect to R_1 above are also suitable candidate monomers for use in this invention.

Acrylates, and methacrylates especially, are particularly interesting monomers for use in this invention. Such compounds are generally of the formula:

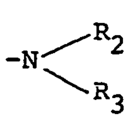


wherein R_5 or R_6, or both, are selected from the group consisting of -H; $-CH_3$; $-C_2H_5$ and

 ; and R_7 is selected from the group consisting of (1) -OH; (2) $O-R_8$, wherein R_8 is 1 to 18 carbon alkyl or aralkyl, aryl or -OH, -Cl, -F, $-NH_2$, $=NO_2$ or $-SO_4$ substituted aralkyl or aryl; (3)

 , R_2 and R_3 being as defined above; (4) -NCO; or (5) -CN.

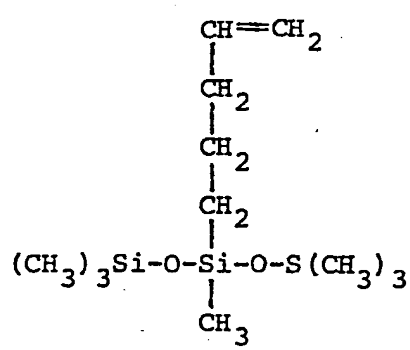
Vinyl ethers, as a class, having a wide range of non-vinyl moiety components are highly suitable monomers for use in this invention. Included are such compounds as $C{=}C{-}O{-}R_8$ wherein R_8 is selected from a group consisting of aryl and 1-18 carbon alkyl and aralkyl, which may be substituted with one or more substituents selected from the group consisting of -OH, -Cl, -F, $-NH_2$,

 wherein R_2 and R_3 are as defined above, $-NO_2$ and $-SO_4$.

Acrylamides such as dimethylaminoethyl acrylamides, dimethylaminopropyl acrylamide and analogs of the above, are suitable for use in this invention.

Suitable methacrylamides include dimethylaminopropyl methacrylamide, dimethylaminoethyl methacrylamide, and the diethylamino and methylethylamino analogs of the above. Difunctional methacrylamides are also contemplated, e.g., aminoethylaminoethyl dimethacrylamide, aminopropylaminoethyl dimethacrylamide, etc., and aminopropylpiperazinepropyl dimethacrylamide.

It is not necessary that the entire polymer be formed via polymerization of "vinyl" group, i.e., aliphatic carbon-carbon double bond; indeed, any polymer which is derived from any monomer or group of monomers or prepolymers in which some or all polymerization occurs via vinyl polymerization may be used within the content of this invention. For example, some silicone monomer systems include polymerizable vinyl group monomers, for example



Such monomers may be a minor part of the total monomer system, but provide reactive sites for bonding polymerizable vinyl group containing asepticizing agents into the polymer to prevent any leaching of the asepticizing agent. Di-vinyl functional monomers of this class serve as cross-linking agents.

Similarly, this invention is applicable to the POLYCON (Trademark) type lens in which both acrylate and silicone polymerization may occur.

Asepticizing agents, generally, i.e., bactericides, fungicides, viricides, anti-rickettsiae agent, to which a polymerizable group is attached or can be attached directly or indirectly, may be used within the principle of this invention, irrespective of the particular nature of the asepticizing agent, so long as the asepticizing agent does not interfere with the polymerization process or destroy the optical properties of the lens polymer. These constraints are, of course, easily determined by simply empirical observation and experimentation.

Polymeric drugs formed by polymerization of vinyl groups have been the subject of investigation[2,13,14,15,16,18,30] and polymerized quaternary ammonium surfactants and chromophores[13-14,18,21,23-26,32,39,73,78-79,81-82] are known. These materials, however, generally are water soluble liquids and, therefore, have no applicability in the context of the present invention, other than to illustrate the known principals of vinyl polymerization.

Fungicidal paints[91,102], metal-silicon bond compounds[92] and biologically active polymers generally are known.

While the present invention is not restricted to any particular class or classes of asepticizing agents, physiological compatability of the asepticizing agents with body tissue and fluids is, of course, a prerequisite. However, the constraint imposed by the necessity for physiological compatability is less severe in respect to the asepticizing agents in this invention than if the same asepticizing agents were contemplated for use in unpolymerized, unbound form. Generally, asepticizing agents bound as described in this invention will be less irritating and more compatible with body fluids and tissues

than the unbonded asepticizing agents would be. The asepticizing agents should be effective within the general pH range of about 6.5 to about 8.5.

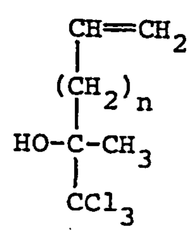
Since differing asepticizing agents exhibit biocidal or biostatic (inhibiting growth of microorganisms) effectiveness at differing concentration levels, only general guidelines for the amount of asepticizing agents which should be polymerized into the lens polymer can be given. For a given asepticizing agent, it is a simple matter to extrapolate from the biologically effective concentration of the asepticizing agent in its free form to the projected concentration of the bonded asepticizing agents which should be included in the polymer. Generally speaking, asepticizing agent concentration will range from about 0.001 to 10%, by weight, of the lens polymer and, most commonly, will fall within the 0.1 to 3% weight concentration range. Generally speaking, the same concentration of asepticizing agent which is effective as a biocide in solution will also be effective as a biostatic asepticizing agent in the same concentration in the lens. Since the asepticizing agents tend to be less irritating when bonded to the polymer, however, it is possible for the concentration of asepticizing agent in the polymer to be increased, e.g., to from 3 to 10 times the optimally effective biocidal concentration of the asepticizing agent in the unbonded form in solution. Ultimately, the optimum biologically effective concentration of asepticizing agent in the polymer must be determined through established biological screening techniques, which are well established in clinical and developmental work.

Exemplary of asepticizing agents having bacteriacidal and bacteriastatic effects which are suitable for use

within the principals of this invention are chlorobutanol, hexachlorophene, chlorophenesin, benzylkonium compounds generally, sulfa derivatives, organo-mercurial compounds, hydroxyquinolin, substituted phenols generally, and analogs of these classes of compounds.

Trichlorotertiary butyl alcohol exemplifies a class of compounds which are suitable for use in lenses according to the invention; indeed, the present invention makes possible the use of this compound and analogs thereof as an asepticizing agent in connection with eye tissue notwithstanding that this class of compounds cannot be used alone without undue irritation to many users. Heretofore, for example, trichlorobutanol could not be used as an asepticizing agent for hydrogel soft contact lenses or as a preservative in hydrogel soft contact lens solutions because it concentrates in the hydrogel and leaches into the tear fluid irritating and damaging eye tissue. When used according to this invention, however, these compounds retain their physiological activity but are non-irritating or substantially less irritating to eye tissue than the compounds used alone.

The following compounds are exemplary of this class of compounds as modified for use in accordance with this invention:

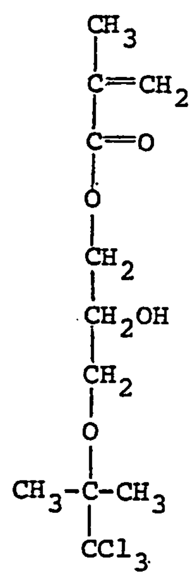


wherein n is a positive integer of from 1 to 10.

It is desirable to space the biologically acrive moiety from the polymerizable vinyl group to minimize

steric hindrance and interference with the polymerization process and also to enhance the activity of the biologically active portion of the molecule. Generally, spacer methyl, or other, groups of from 1 to 3 or 4 such groups are quite satisfactory, although spacer methyl groups up to 10 carbon atoms may conveniently be used. There is no reason why high molecular weight spacer moieties could not be used, within the limits of steric hindrance, but there is no apparent advantage in greater spacing.

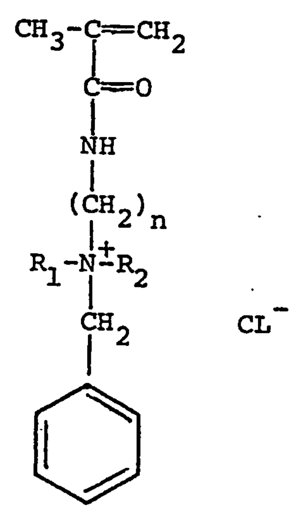
Chlorobutanol may also be reacted with glycidyl methacrylate to produce the following polymerizable vinyl group containing compounds which is suitable for use in this invention:



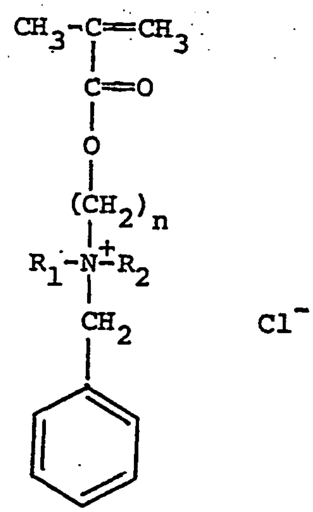
Other reactive hydroxy containing aseptic agents with the same or other epoxy reactive group containing compounds which also include a polymerizable vinyl group to produce polymerizable aseptic agents according to this invention.

Benzylkonium compounds, which may be both bacteriastatic and fungastatic asepticizing agents, may

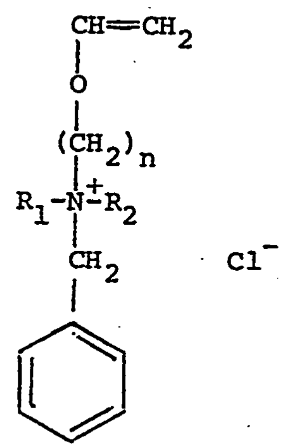
also be modified to include a polymerizable vinyl group for use in accordance with this invention. Heretofore, benzylkonium compounds could not be used in hydrogel soft lens because they concentrate in the hydrogel and leach into the eye and may cause severe tissue damage. This difficulty may be overcome by polymerizing the benzylkonium to the lens polymer to thereby bond the benzylkonium group to the polymer and prevent leaching with consequent irritation or damage to the eye. Exemplary of such benzylkonium compounds include:



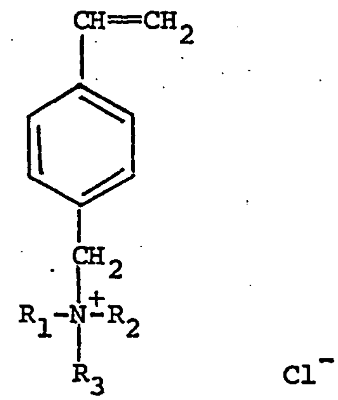
wherein R_1 and R_2 are alkyl groups having from 1 to 18 carbon atoms, and most commonly is methyl, and n is a positive integer of from 1 to 18.



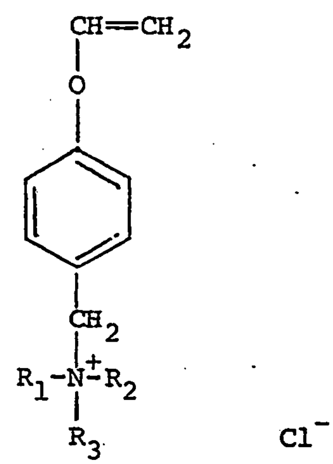
wherein R_1 and R_2 are alkyl groups having from 1 to 18 carbon atoms, and most commonly is methyl, and n is a positive integer of from 1 to 18.



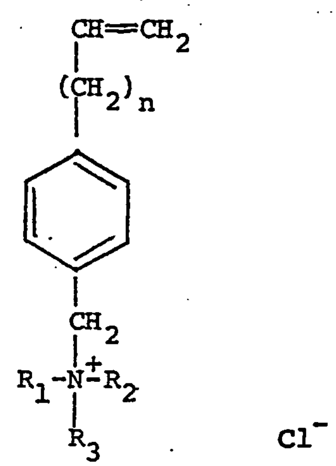
wherein R_1 and R_2 are alkyl groups having from 1 to 18 carbon atoms, and most commonly is methyl, and n is a positive integer from 1 to 18.



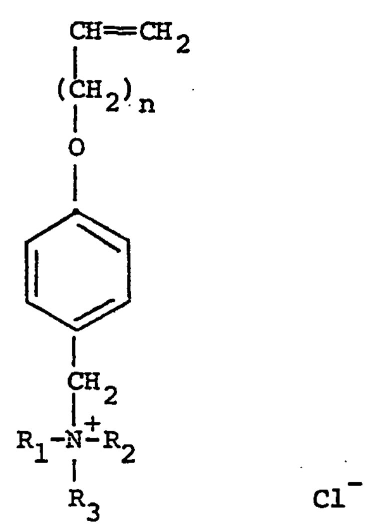
wherein R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.



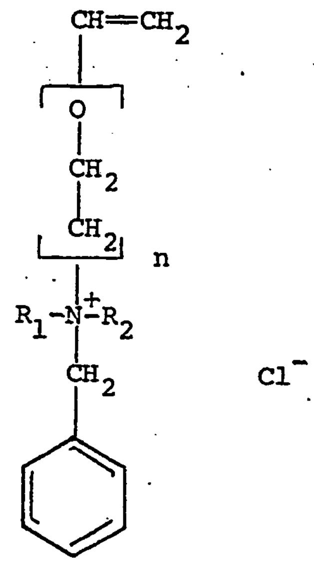
wherein R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.



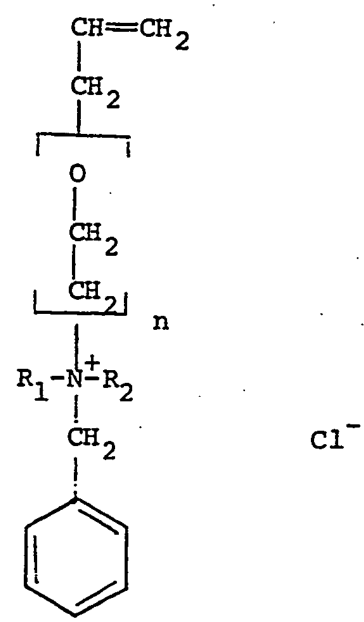
wherein n is a positive integer from 1 to 10 and R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.



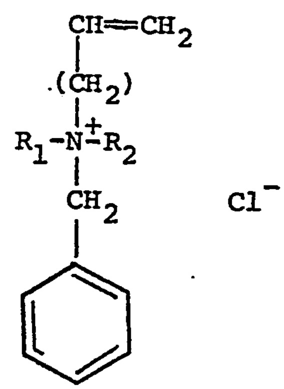
wherein n is a positive integer from 1 to 10 and R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.



wherein n is a positive integer of from 1 to 2000 and R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.

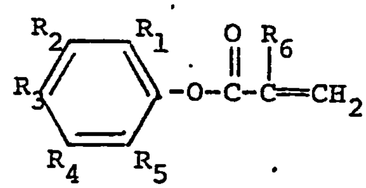


where n is a positive integer of from 1 to 2000 and R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.

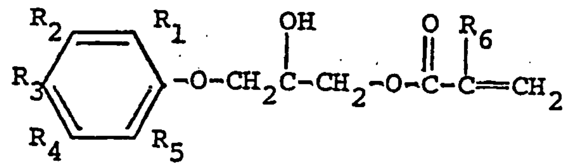


wherein n is a positive integer from 1 to 10 and R_1, R_2 and R_3 are 1 to 18 carbon alkyl and, preferably, where two of R_1, R_2 and R_3 are methyl and one of R_1, R_2 and R_3 is a 8 to 18 carbon alkyl.

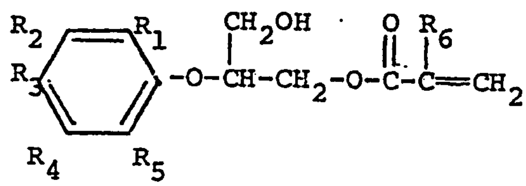
Substituted phenols are suitable antibacterial asepticizing agents, exemplary of which are:



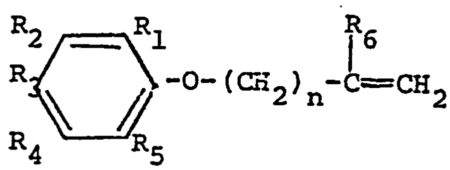
wherein R_1, R_2, R_3, R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl.



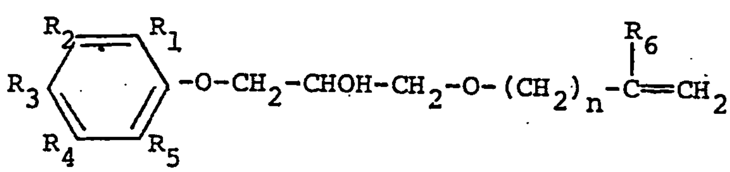
wherein R_1, R_2, R_3, R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl.



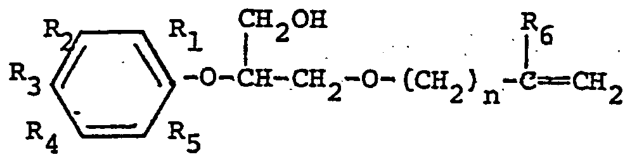
wherein R_1, R_2, R_3, and R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl.



wherein R_1, R_2, R_3, R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl and n is zero or a positive integer of from 1 to 10.

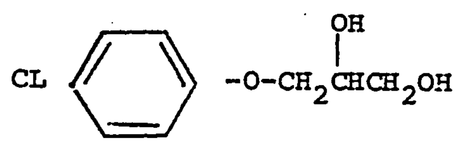


wherein R_1, R_2, R_3, R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl and n is zero or a positive integer of from 1 to 10.



wherein R_1, R_2, R_3, R_4 and R_5 are halide, hydrogen, or 1 to 9 alkyl or alkoxy, at least one of R_1 through R_5 being halide, and R_6 is hydrogen or methyl and n is zero or a positive integer of from 1 to 10.

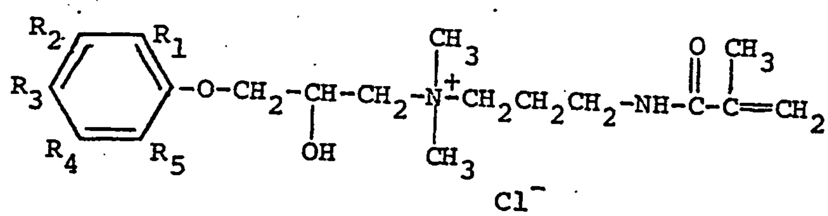
Chlorphenesin,

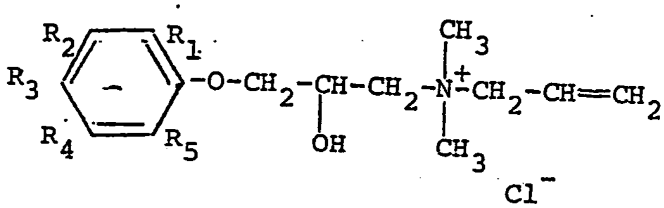


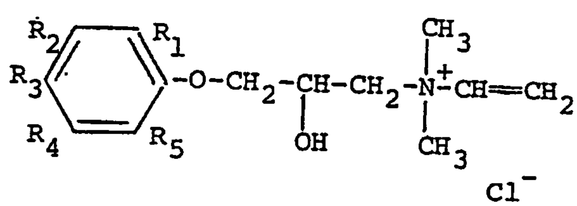
prepared by condensing equamolar amounts of p-chlorophenol and glycidol, and its plural chloro-substituted analogs have antifungal properties which, by the methods of this invention, e.g., the addition of the foregoing vinyl group containing derivatives, antigungal activity can be imparted to solid polymeric contact lenses.

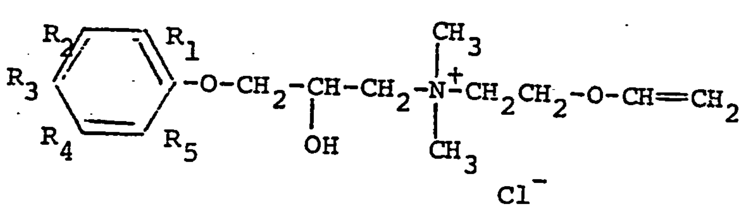
The microbiological activity of two classes of biocidal asepticizing agents can be imparted to contact lenses by polymerizing with the lens polymer asepticizing agents having different or plural biocidal characteristics. For example, the lens forming monomer can be copolymerized with polymerizable vinyl group containing quaternary ammonium compounds and vinyl group containing chlorphenesin compounds. These two classes of compounds are selected merely to exemplify the concept of including two asepticizing agents in a single lens forming polymer. Two biologically active agents can also be combined into one monomer containing a polymerizable vinyl group. As an example of this approach, a chlorphenesin-quaternary ammonium

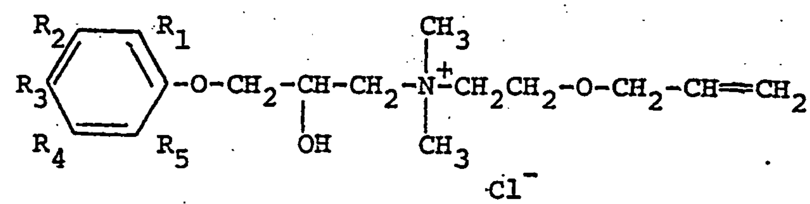
polymerizable vinyl group monomer can be prepared and copolymerized with the lens polymer. Merely exemplary of this approach to building non-leachable asepticizing agents into lens polymers are the following compounds which contain polymerizable vinyl group and the two classes of asepticizing agents referred to:





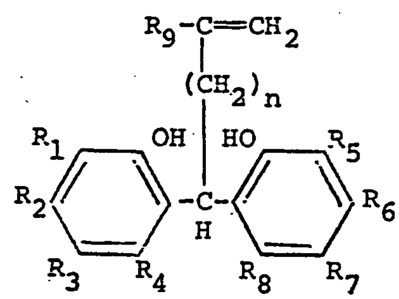


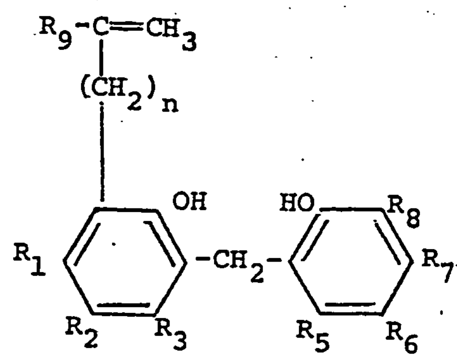


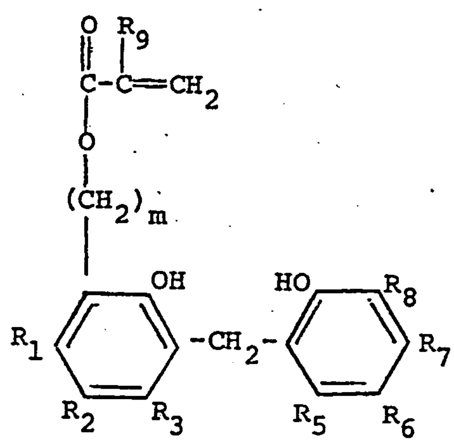


wherein at least one of R_1, R_2, R_3, R_4 and R_5 is a halogen and remainder is hydrogen, hydroxy, halogen, or lower 1 to 10 carbon alkyl.

Hexachlorophene, a recognized bactericide, may be modified by the addition of the polymerizable vinyl group and included in polymers according to this invention. Examples of polymerizable analogs of hexachlorophene include:

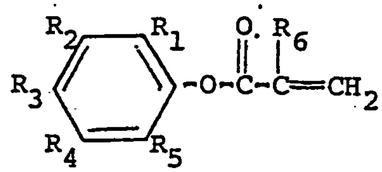




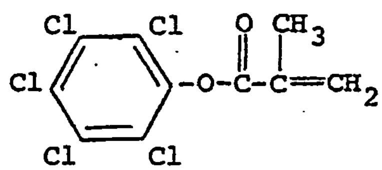


wherein n is a positive integer from 1 to about 18, m is zero or a positive integer from 1 to about 18, R_1 through R_8 are halogen or lower, 1 to 10 carbon, alkyl or alkoxy, at least one of R_1 to R_3, and at least one of R_5 to R_8 being halogen, the vinyl containing substituent in the next preceding two structures being attached to either phenyl ring at the ortho, meta or para positions with respect to the hydroxy groups, R_9 being hydrogen, halogen or 1 to 4 carbon alkyl.

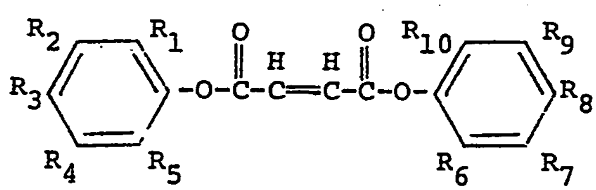
Biocidally effective halogen substituted phenyl compounds generally are satisfactory condidates for utilization in this invention. These classes of compounds would include the following:

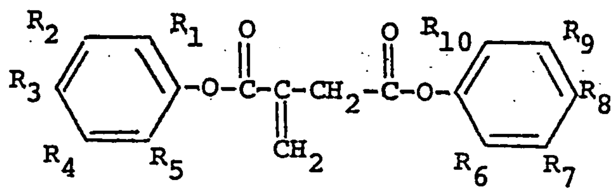


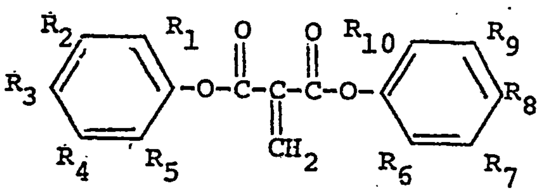
wherein at least one of R_1 through R_5 is halogen and each of R_1 through R_5 are halogen, hydroxy, hydrogen or lower 1 to 10 carbon, alkyl or alkoxy, and R_6 is hydrogen, halogen or 1 to 4 carbon alkyl, e.g., pentachlorophenyl methacrylate,

 ,

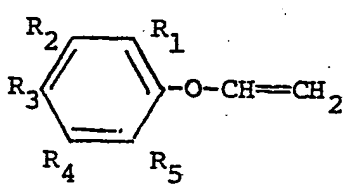
and analogous acrylates, crotonates and maleates;

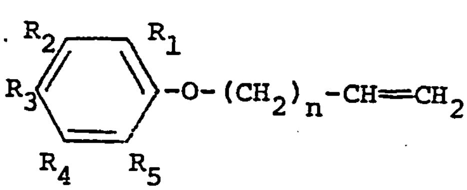


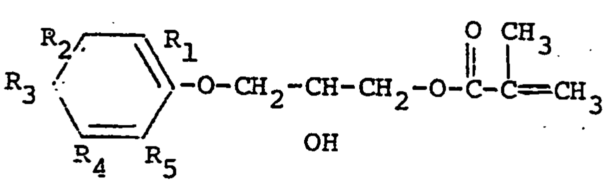




wherein at least one of R_1 to R_5 and of R_6 to R_{10} is halogen and each of R_1 to R_{10} is hydrogen, hydroxy, halogen or lower, 1 to 10 carbon, alkyl or alkoxy; and vinyl, allyl, and crotonyl and glycidyl ethers, e.g.,



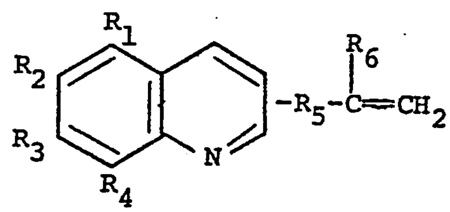




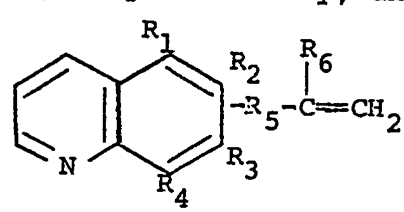
wherein at least one of R_1 to R_5 is halogen, and each of R_1 to R_5 is hydrogen, hydroxy, halogen or lower 1 to 10 carbon alkyl or alkoxy.

Other classes of biocidal asepticizing agents which can be used in accordance with this invention include:

Quinolinol derivatives, to which a polymerizable group has been attached:

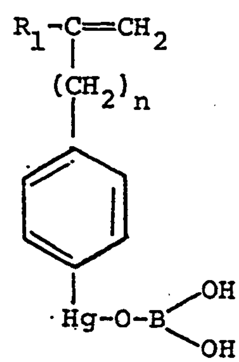


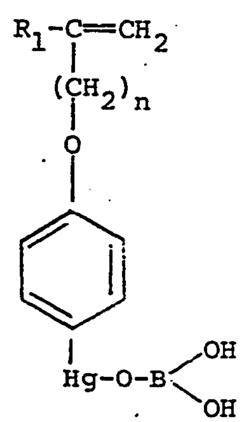
wherein at least one of R_1 to R_4 is hydroxyl, and each of R_1 to R_4 is hydrogen, hydroxy, halogen or lower, 1 to 10 carbon, alkyl or alkoxy, and

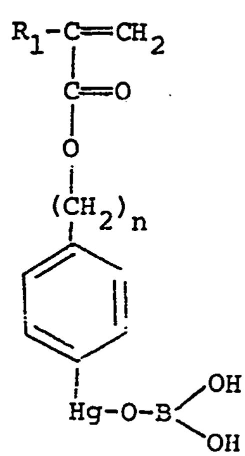


wherein one of R_1 to R_4 is vinyl group containing substituent, at least one of R_1 to R_4 is hydroxyl and the remaining R_1 to R_4 positions are hydrogen, hydroxy, halogen or 1 to 4 carbon alkyl.

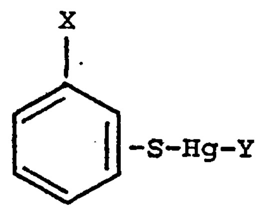
Organo-mercury compounds which have been modified to include a polymerizable vinyl group:







wherein R_1 is halogen, hydrogen or 1 to 4 carbon alkyl, and n is zero or a positive integer of 1 to 10, and polymerizable vinyl group containing thio-mercury compounds, e.g.,



where X is a protonic acid group, or salt thereof, selected from the group consisting of:

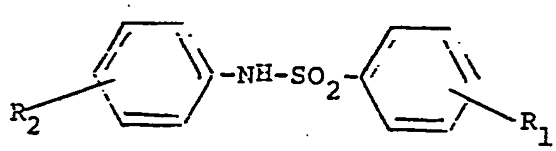
$$-\overset{\overset{\displaystyle O}{\|}}{C}-O-H \quad \text{and} \quad -\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-O-H$$

and Y is a polymerizable vinyl group containing substituent selected from the group consisting of

$$-(CH_2)_n-\overset{\overset{\displaystyle R_1}{|}}{C}{=}CH_2 \quad \text{and} \quad -(CH_2)_n-O-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle R_1}{|}}{C}{=}CH_2 \quad ,$$

n being zero or a positive integer of 1 to 10, and R_1 being hydrogen, halogen, or 1 to 4 carbon alkyl.

Sulfa drugs generally, see THE MERCK INDEX, 9th Ed., pp. 1150-1159, to which a polymerizable vinyl group has been attached, for example:



,

and nitrogen heterocyclic analogs thereof, wherein one of R_1 and R_2 is a polymerizable vinyl group containing substituent selected from the group consisting of:

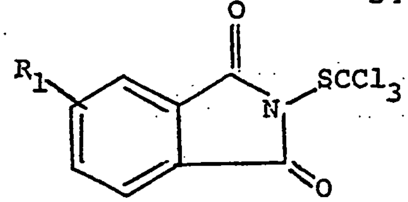
$$-(CH_2)_n-\overset{\displaystyle R_3}{\overset{|}{C}}{=}CH_2\ ,\qquad -O-(CH_2)_n-\overset{\displaystyle R_3}{\overset{|}{C}}{=}CH_2\ ,$$

$$-O-\overset{\displaystyle O}{\overset{\|}{C}}-(CH_2)_n-\overset{\displaystyle R_3}{\overset{|}{C}}{=}CH_2\ ,\quad \text{and} \quad -\overset{\displaystyle H}{N}-\overset{\displaystyle O}{\overset{\|}{C}}-(CH_2)_n-\overset{\displaystyle R_3}{\overset{|}{C}}{=}CH_2$$

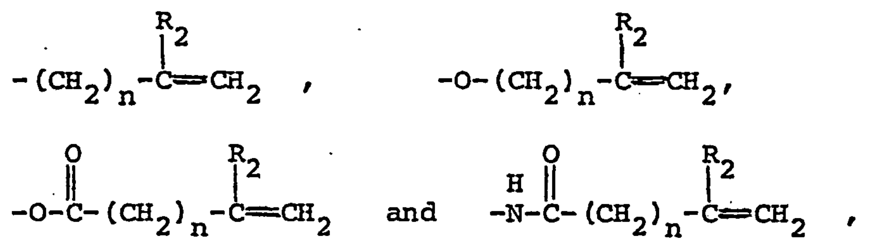
R_3 being hydrogen, halogen or 1 to 4 carbon alkyl, and n being zero or a positive integer of 1 to 10.

Polyvinyl amine-vinyl sulfonate sodium salt copolymers, as described by Dawson et al[13] may be converted to substituted sulfanilamides, and then graft polymerized with acrylic monomers as described by Smets et al[90]. By this means, a water-soluble sulfanilamide containing polymer may be polymer bound into a hydrogel lens polymer to provide antibacterial properties. By the proper choice of substituents, anti-fungal, anti-viral, anti-rickettsial and enzyme inhibitory properties may also be incorporated.

The problem of fungus infusion into contact lenses may be eliminated by including a polymer bound anti-fungus type agent in the polymer network. CAPTAN® and its analogs may be used to produce a polymer network with a fungistatic agent bound to the polymer backbone. Examples of these asepticizing monomers include:

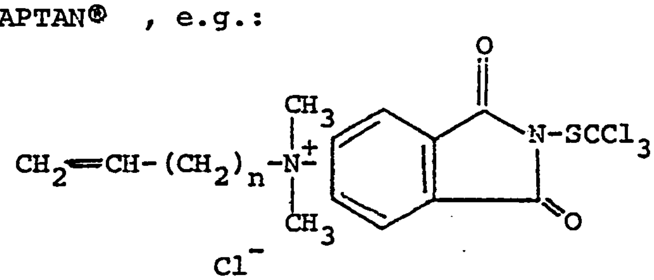


wherein R_1 is a polymerizable vinyl group containing substituent selected from the group consisting of:



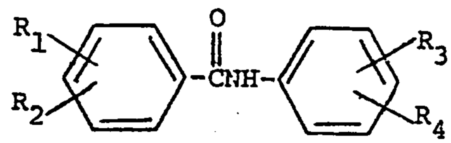
R_2 being hydrogen, halogen or 1 to 4 carbon alkyl, and n being zero or a positive integer of 1 to 10.

Quaternary ammonium - polymerizable vinyl derivatives of CAPTAN®, e.g.:



wherein n is zero or a positive integer of 1 to 10.

Salicylanilide derivatives which include a polymerizable vinyl group, e.g.,:



wherein R_1 or R_3 is a polymerizable vinyl group containing substituent selected from the group consisting of:

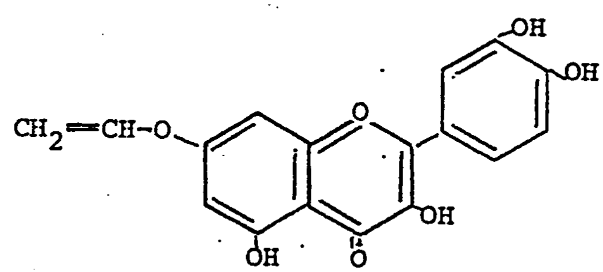
$$-(CH_2)_n-\underset{}{\overset{R_5}{\overset{|}{C}}}=CH_2, \qquad -O-(CH_2)_n-\overset{R_5}{\overset{|}{C}}=CH_2$$

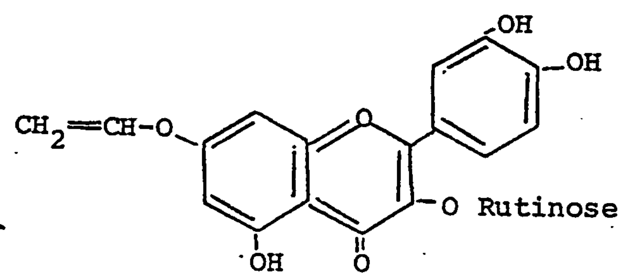
$$-O-\overset{O}{\overset{\|}{C}}-(CH_2)_n-\overset{R_5}{\overset{|}{C}}=CH_2 \quad \text{and} \quad -\overset{H}{N}-\overset{O}{\overset{\|}{C}}-(CH_2)_n-\overset{R_5}{\overset{|}{C}}=CH_2 ,$$

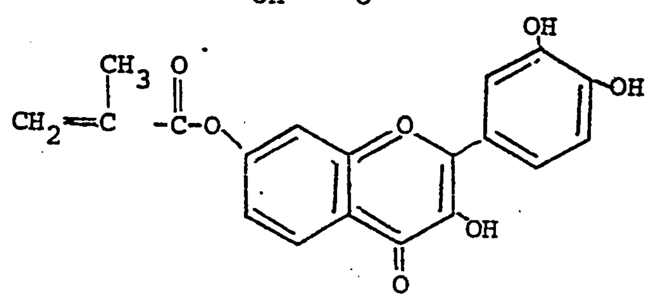
R_5 being hydrogen, halogen or 1 to 4 carbon alkyl, n being zero or a positive integer of 1 to 10, one of R_1 to R_4 is hydroxyl, the remainder of R_1 to R_4 being hydrogen, hydroxyl, halogen or 1 to 7 carbon alkyl or alkoxy.

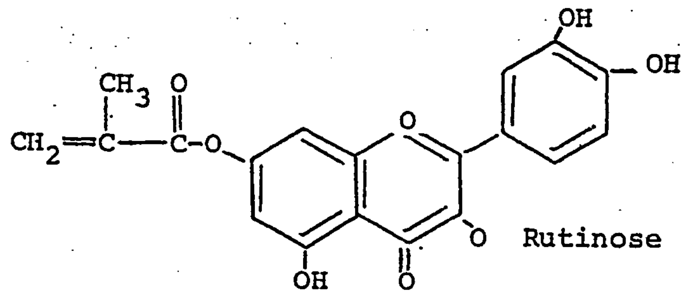
Adamantine derivatives such as adamantaryl methacrylate, adamantaneamine-glycidyl methacrylate adduct, adamantane carboxylic acid chloride, allyl adamantaneamine hydrochloride and methacryloxyethyl adamantane carboxylate add viricidal activity to lenses.

Suitable enzyme inhibibors are the bioflavonoids quercetin and rutin modified with polymerizable vinyl groups in the form of alkenyl ethers or esters, and then copolymerized with acrylic monomers to give a polymer bound enzyme inhibitor to prevent enzyme attack of hydrogel contact lenses; for example:


OH
OH
CH2=CH-O
O
OH
OH
O


OH
OH
CH2=CH-O
O
O Rutinose
OH
O


OH
CH3
O
OH
CH2=C
-C-O
O
OH
O



Antirickettisial effectiveness is built into lens polymers by copolymerization of analogous derivatives of chloroamphenicol.

Lens blanks are prepared by mixing monomers and asepticizing agent conventionally and placing the mixture in an oven to begin the polymerization. Polymerization is carried out conventionally between 40°C and 100°C. Blanks are then annealed for several hours at 85°C, and lenses are cut and polished. In the case of soft lenses, the polished lenses are hydrated in saline solution to form hydrated hydrogel soft contact lenses.

The following examples are for illustration only and are not to be construed as limiting the scope of the invention:

<u>Example 1</u>

2-hydroxyethyl methacrylate	50.00 g
CAPTAN ® (Chevron Chemical Co., recrystallized from 1,1,1-trichloroethane)	0.03 g

The above were preheated together for 2 2/3 hours at a temperature of 116°C to dissolve the Captan in the 2-hydroxyethyl methacrylate.

Methyl methacrylate	1.50 g
Triethylene glycol dimethacrylate	0.50 g

Methyl methacrylate and triethyleneglycol dimethacrylate were added and heating was continued for one hour at 89-93°C.

Five drops of 2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245 U.S. Peroxygen Div., Whitco Chem. Co.] was added and the mixture was blended and cured 4 1/2 hours at 90-106°C. The lens blanks were clear and of good optical quality. The hydration level was 34.5%.

Example 2

2-hydroxyethyl methacrylate	100.0 g
Methyl methacrylate	3.0 g
Triethyleneglycol dimethacrylate	1.0 g
Benzalkonium chloride salt of dimethylaminopropyl methacrylamide	0.20 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	10 drops

The above were blended thoroughly and cured at 85-95°C for two hours and 95-100°C for two hours. The lens blanks were clear and of good optical quality.

Example 3

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.0 g
Triethyleneglycol dimethacrylate	1.0 g
Benzalkonium chloride salt of dimethylaminoethyl methacrylate	0.20 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	10 drops

The above were blended thoroughly and cured at 85-95°C for two hours and at 95-100°C for two hours. The lens blanks were clear and of good optical quality.

Example 4

2-hydroxyethyl methacrylate	100.0 g
Methyl methacrylate	3.0 g
Triethyleneglycol dimethacrylate	1.0 g
Benzalkonium chloride salt of dimethylaminoethyl vinyl ether	0.20 g

2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	10 drops

The above were blended thoroughly and cured at 85-95°C for two hours and 90-100°C for two hours. The lens blanks were clear and of good optical quality.

Example 5

2-hydroxyethyl methacrylate	100.0 g
Methyl methacrylate	3.0 g
Triethyleneglycol dimethacrylate	1.0 g
Benzalkonium chloride salt of 1-dimethylamino dodecane and vinyl benzyl chloride	0.20 g
2-5-dimethylhexane-2,5-diper-2-ethyl hexoate	10 drops

The above were blended thoroughly and cured at 85-95°C for two hours. The lens blanks were clear and of good optical quality.

Example 6

2-hydroxyethyl methacrylate	100.0 g
Methyl methacrylate	3.0 g
Triethyleneglycol dimethacrylate	1.0 g
5-hydroxy-5-trichloromethyl hexene-1	0.20 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	10 drops

The above were thoroughly blended and cured for two hours at 85-95°C and two hours at 95-100°C. The lens blanks were clear and of good optical quality, giving lenses of optical quality equal to the forumulation without the asepticizing agent.

Example 7

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.54 g
Pentachlorophenyl methacrylate	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	5 drops

The above mixture was blended until all of the pentachlorophenyl methacrylate dissolved. The mixture was placed in polyethylene molds and cured at 96°C for 1 hour and 40 minutes, and annealed for 3 1/2 hours at 85°C.

The lens blanks had a hardness of 85-86D on top and 86-88D on the bottom. Two lenses were made, one had an equilibrium hydration level of 33.8% and the other 35.6%, the optics of both lenses were very good.

Example 8

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Pentachlorophenyl methacrylate	0.50 g
N-Adamantanyl methacrylamide	0.50 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	5 drops

The above were thoroughly mixed, with care to dissolve all of the solid components. The mixture was placed in molds in the oven at 94°C, and cured for 1 hour and 45 minues at 94°C and annealed for 4 hours at 88°C.

Example 9

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Pentachlorophenyl methacrylate	0.10 g
N-Adamantanyl methacrylamide	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care to dissolve all of the solid components. The mixture was placed in molds in the oven at 95°C and cured for 1 hour and 45 minutes at 95°C and annealed for four hours and 15 minutes at 88°C. The lens blanks had a hardness of 83-88, and gave lenses with a hydration level of 32.4%.

Example 10

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.00 g
Triethyleneglycol dimethacrylate	1,00 g
Quercetin methacrylate	0.05 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	10 drops

The above were thoroughly mixed with care to dissolve all of the solid component. The mixture was placed in molds in the oven at 95°C and cured for one hour and 30 minutes at 95°C and annealed for two hours at 85°C. The blanks had a hardness of 84-86D and gave lenses with a hydration level od 34.5% with a yellow cast.

Example 11

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.00 g
Triethyleneglycol dimethacrylate	1.00 g

Chloramphenicol methacrylate	0.10 g
2,5-dimethylhexane-2,5,-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	10 drops

The above were thoroughly mixed with care to dissolve all of the solid component. The mixture was placed in molds in the oven at 95°C and cured for one hour and 30 minutes at 95°C and annealed for two hours at 85°C. The blanks had a hardness of 84-86D and gave lenses with a hydration level of 34.0%.

Example 12

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
1-adamantaneamine-glycidyl methacrylate adduct	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were mixed thoroughly with care to dissolve all of the adamantane derivative. The mixture was placed in molds in the oven at 95°C and cured for one hour and 53 minutes at 95-96°C and annealed for three hours and 30 minutes at 86°C. The blanks had a hardness of 76-87D and gave lenses with a hydration level of 35.9%.

Example 13

2-hydroxyehtyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
1-Adamantane carboxylic acid chloride	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	6 drops

The above were mixed thoroughly, with care to dissolve all of the adamantane derivative. The mixture was placed in molds in the oven at 96°C and cured for one hour and 52 minutes at 96°C, and annealed for three hours and 30 minutes at 86°C. The blanks had a hardness from 80-87D and gave lenses with a hydration level of 31.4%.

Example 14

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
N-1-Adamantanyl methacrylamide	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care, to dissolve all of the adamantane derivative. The mixture was placed in molds in the oven at 95°C and was cured for one hour and 45 minutes at 94-95°C and annealed for three hours and 30 minutes at 87°C. The blanks had a hardness of 83-88D and gave lenses with a hydration level of 30.6%.

Example 15

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
N-Allyl-1-Adamantaneamine Hydrochloride	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed with care to dissolve the solid component. The mixture was placed in molds in the oven at 95°C and cured for one hour at 95°C. The temperature was raised to 110°C over a period of 8 minutes and the cured

continued at 110°C for one hour. The blanks were annealed at 85°C for eight hours. The blanks had a hardness from 77-85D and gave lenses with a hydration level of 33.5%.

Example 16

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Methacryloxyethyl adamantane-carboxylate	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S Peroxygen Div., Whitco Chem. Co.)	6 drops

The above were thoroughly mixed, with care, to dissolve all of the adamantane derivative. The mixture was placed in molds in the oven at 95°C, and cured for one hour and 45 minutes at 95°C, and annealed for four hours and 15 minutes at 88°C. The lens blanks had a hardness of 84-88D and gave lenses with a hydration level of 35.5%.

Example 17

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Methacrylamidopropyl-dimethylbenzyl ammonium chloride	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were mixed thoroughly with care to dissolve all of the benzalkonium derivative. The mixture w-s placed in molds in the oven at 93°C and cured for one hour and 46 minutes at 93°C, and annealed for four hours at 86°C. The blanks had a hardness of 81-87D and gave lenses with a hydration level of 34.7%.

Example 18

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Methacrylamidopropyl-dimethylbenzyl ammonium chloride	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were mixed thoroughly with care to dissolve all of the benzalkonium derivative. The mixture was placed in molds in the oven at 93°C and cured for one hour and 46 minutes at 93°C, and annealed for four hours at 86°C. The blanks had a hardness of 81-87D and gave lenses with a hydration level of 34.7%.

Example 19

2-hydroxyethyl methacrylate	20.00 g
Methyl methacrylate	0.60 g
Triethyleneglycol dimethacrylate	0.20 g
Allyl dimethyl benzalkonium chloride	0.20 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	2 drops

The above were thoroughly mixed, with care to dissolve all of the benzalkonium derivative. The mixture was placed in molds in the oven at 94°C and cured for one hour and 45 minutes at 94°C and annealed for three hours and 30 minutes at 87°C. The blanks had a hardness of 87D and gave lenses with a hydration level of 27.0%.

Example 20

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g

Triethyleneglycol dimethacrylate	0.50 g
Vinyl benzyl dimethyl dodecyl ammonium chloride	0.25 g
2,5 dimethyl hexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were mixed thoroughly with care to dissolve all of the benzalkonium compound. The mixture was placed in molds in the oven at 95°C and cured one hour and 46 minutes at 95°C. The blanks wer annealed for eight hours at 85°C. The blanks had a hardness of 76-87D and gave lenses with a hydration level of 30.8%.

Example 21

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
5-hydroxy-5-trichloromethyl hexene-1	0.25 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care to dissolve all of the hexene derivative. The mixture was placed in molds in the oven at 93°C and cured for one hour and 45 minutes at 93°C and annealed for four hours at 86°C. The blanks had a hardness of 82-87D and gave lenses with a hydration level of 34.7%.

Example 22

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
2-methacryloxyethyl-2,22-trichloro-5-butyl carbonate	0.25 g

2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care to dissolve all of the carbonate derivative of chlorobutanol. The mixture was placed in molds in the oven at 96°C and cured for one hour and 45 minutes at 95-96°C, and annealed for three hours and 30 minutes at 85°C. The blanks had a hardness of 80-88D and gave lenses with a hydration level of 30.5%.

Example 23

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.00 g
Triethyleneglycol dimethacrylate	1.00 g
N-vinylphenylsulfanilamide	0.05 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	10 drops

The above were thoroughly mixed, with care, to dissolve all of the solid component. The mixture was placed in molds in the oven at 95°C and cured for one hour and 45 minutes at 95°C and annealed for four hours at 85°C. The blanks had a hardness of 85-86D and gave lenses with a hydration level of 33.8%.

Example 24

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
N-4-vinylphenylsalicylamide	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed with care to dissolve all of the solid component. The

mixture was placed in molds in the oven at 95°C and cured for one hour and 45 minutes at 95°C and four hours at 85°C. The blanks had a hardness of 85-87D and gave lenses with a hydration level of 34.0%.

Example 25

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.00 g
Triethyleneglycol dimethacrylate	1.00 g
Vinylphenylmercury borate	0.10 g
N-methacryloxyethyl ethylene-diamine triacetic acid di sodium salt	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	10 drops

The above were mixed thoroughly with care to dissolve all of the solid components. The mixture was placed in molds in the oven at 95°C and cured for one hour and 30 minutes and annealed for two hours at 85°C. The blanks had a hardness of 85-87D and gave lenses with a hydration level of 34.6%.

Example 26

2-hydroxyethyl methacrylate	100.00 g
Methyl methacrylate	3.00 g
Triethyleneglycol dimethacrylate	1.00 g
Vinylphenylmercury borate	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	10 drops

The above were thoroughly blended and then placed in molds in the oven at 95°C and cured for one hour and 30 minutes and annealed two hours at 85°C. The blanks had a hardness of 85-87D and gave lenses with a hydration level of 34.5%.

Example 27

2-hydroxyethyl methacrylate	50.00 g
Methyl methacrylate	1.50 g
Triethyleneglycol dimethacrylate	0.50 g
Pentachlorophenyl methacrylate	0.25 g
2,5-dimethylhexane-2,5-diper-2-ehtyl hexoate (U.S.P. 245, U.S Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care to dissolve all of the pentachlorophenyl methacrylate. The mixture was placed in molds in the oven at 96°C and cured for one hour and 40 minutes at 96°C and annealed for three hours and 30 minutes at 85°C. The blanks had a hardness of 85-88D and gave lenses with a hydration level of 35.6%.

Example 28

2-hydroxyethyl methacrylate	28.00 g
Methoxyethyl methacrylate	20.10 g
Methacrylic acid	4.09 g
Triethyleneglycol dimethacrylate	0.50 g
Pentachlorophenyl methacrylate	0.10 g
N-adamantanyl methacrylamide	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S Peroxygen Div. Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care, to dissolve all of the solid components. The mixture was placed in molds in the oven at 94°C and cured for one hour and 49 minutes at 94°C, and annealed for four hours at 88°C.

Example 29

2-hydroxyethyl methacrylate	50.00 g
Triethyleneglycol dimethacrylate	0.64 g
Pentachlorophenyl methacrylate	0.10 g
N-adamantanyl methacrylamide	0.10 g

2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div. Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care, to dissolve all of the solid components. The mixture was placed in molds in the oven at 94°C and cured for one hour and 48 minutes at 94°C, and annealed for four hours at 88°C.

<u>Example 30</u>

2-hydroxyehtyl methacrylate	50.00 g
Polyvinyl pyrrolidinone (Plasdone K-29-32)	2.50 g
Pentachlorophenyl methacrylate	0.10 g
N-adamantanyl methacrylamide	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed, with care, to dissolve all of the solid components. The mixture was placed in molds in the oven at 94°C and cured for 1 hour and 48 minutes at 94°C, and annealed for four hours at 88°C.

<u>Example 31</u>

2-hydroxyehtyl methacrylate	30.00 g
Methoxyethyl methacrylate	10.00 g
Glycidyl Methacrylate	10.00 g
Pentachlorophenyl methacrylate	0.10 g
N-adamantanyl methacrylamide	0.10 g
2,5-dimethyl hexane-2,5-diper-2-ethyl hexoate (U.S.P. 245, U.S. Peroxygen Div., Whitco Chem. Co.)	5 drops

The above were thoroughly mixed and care was taken to dissolve the solid components. The mixture was placed in the oven at 88°C and cured at 88°C for 30 minutes and at 94°C for five hours.

Example 32

2-hydroxyethyl methacrylate	50.00 g
Styrene	2.40 g
Vinyl pyrrolidinone	10.00 g
Glycidyl methacrylate	1.80 g
Diallyl Di-butyl tin	0.12 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	6 drops

The above mixture was thoroughly mixed and then placed in molds in the oven. The mixture was cured at 83-86°C for one hour and 33 minutes and then annealed at 100°C for 1 hour, 100-125°C for 15 minutes, 125°C for 1 hour, 125-162°C for 30 minutes. The lens blanks were clear, had a dry hardness 84-86, lenses had a hydration level of 31.8%, and good optical quality.

Example 33

2-hydroxyethyl methacrylate	40.00 g
Methyl methacrylate	1.20 g
Triethyleneglycol dimethacrylate	0.40 g
1-trichloromethyl-1-methyl-ethyl methacrylate (Chlorobutanol methacrylate)	0.10 g
2,5-dimethylhexane-2,5-diper-2-ethyl hexoate	1 drop
Tertiary butyl perneodecanoate (Esperox 33m, U.S. Peroxygen Div., Witco Chem. Co.)	4 drops

The above were blended thoroughly and cured at 65-66°C for 2 hours and 10 minutes and then at 100°C for 15 hours. The lens blanks were clear and of good optical quality with a hardness of 88-89D.

Representation samples of the lens blank polymers which include polymerically bound asepticizing agents made in accordance with this invention, as described hereinbefore, were tested and found to exhibit biostatic activity.

Thus, this facet of the invention contemplates virtually any lens polymer which is comprised of the polymerization product of one or more monomers or prepolymers with one or more asepticizing agents wherein polymerization occurs by addition polymerization of ethylenically unsaturated carbon-carbon linkage, i.e., vinyl type polymerization of polymerizable vinyl groups on the lens monomer or prepolymer and on the asepticizing agent.

Alternatives

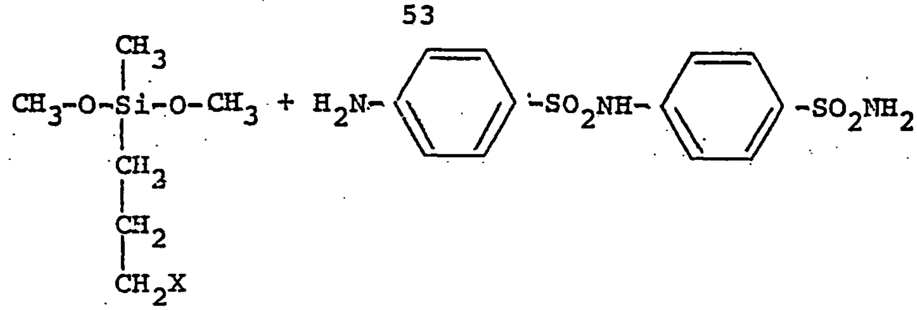
The principles of this invention are applicable to other lens polymer systems generally.

The two non-"vinyl" lens polymers (i.e., not formed by polymerization of an ethylenically unsaturated carbon-carbon, $>C=C<$, bond) of greatest interest are silicone lenses and cellulose acetate-butyrate lenses.

Silicone lenses are siloxane polymers,

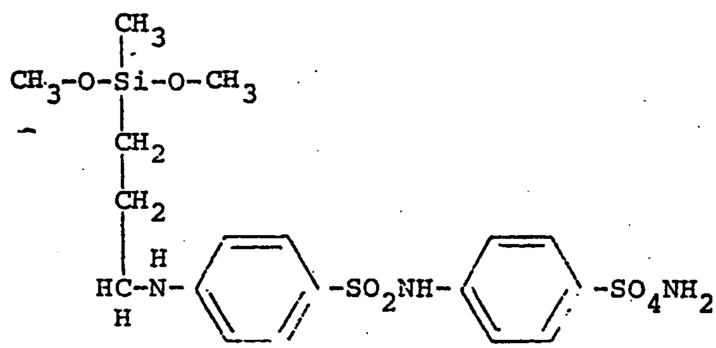
$$\left(-\overset{\displaystyle R_1}{\underset{\displaystyle R_2}{\overset{|}{\underset{|}{Si}}}}-O-\right)_n$$

wherein n is a large positive integer of from under 100 up to several thousand and R_1 or R_2, or both, is typically methyl or phenyl but may often be lower alkyl and halogen substituted lower alkyls. Known silicone monomers may be prepared in modified form to include a reactive group, e.g., -Cl, -OH, $-NH_2$, on one of R_1 or R_2.[92,93,94,95,96,98,99,100,101,102,103,106,108,109,110-111] Asepticizing agents, of the classes described in detail hereinbefore for example, may be reacted, directly, or through an intermediate reactive group, to attach to the siloxane monomer and which become an integrally bound part of the final polymeric lens. The general reaction scheme is typified by the following, in which particular monomers and asepticizing agents are merely exemplary:

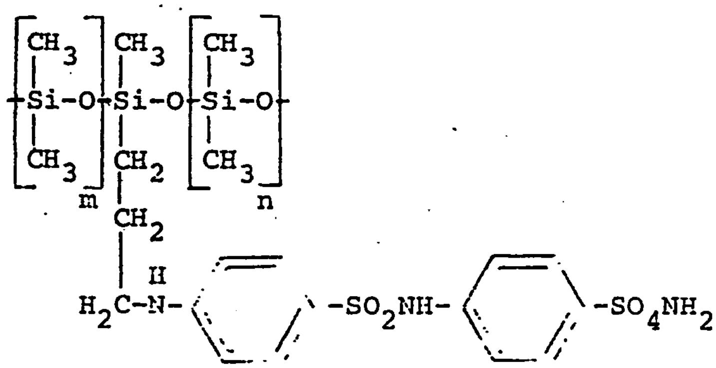


X = Halogen

4'-sulfamoylsulfonil-anilide



which may be polymerized to, e.g.,

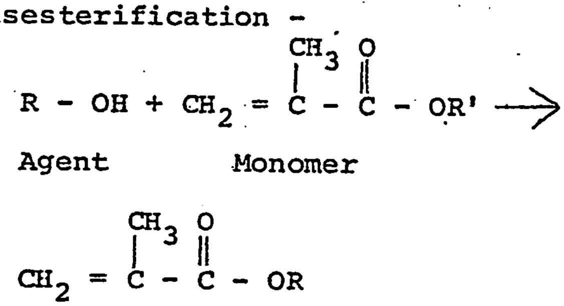


wherein m and n are positive integers of about 10 to several thousand.

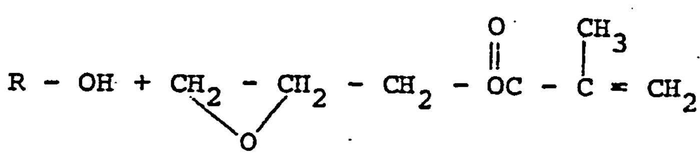
Virtually innumerable variations of this general reaction scheme using silicone monomers and asepticizing agents which include or which may be modified to include reactive groups may be adopted within the scope of this invention.

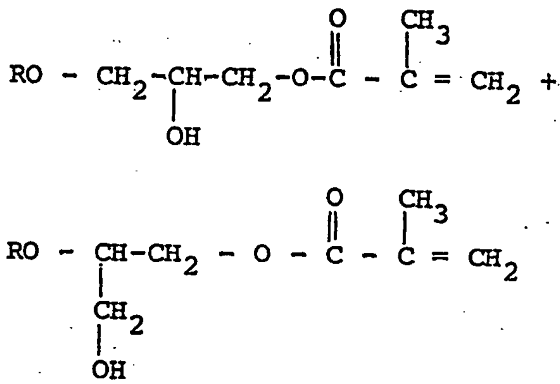
Another specific example is an alcoholic functional group which can be attached to the agent and then used to bond to the monomer through a transesterification reaction. The alcoholic functional group may also, by an epoxy addition reaction, be bonded to a monomer possessing an epoxy group. These reactions are shown below:

Transesterification -



Epoxy addition -





Another example of a functional group would be an isocyanate group which could be reacted with a hydroxy substituted monomer to produce a polymerically bound urethane asepticizing agent. An example would be to react the agent, phenyl isocyanate with a HEMA monomer. With polymerization, the parachlorophenol isocyanate reacts with the HEMA to form a polymerically bound urethane bacteriacide within the polymer matrix of the contact lens.

Another example of a functional group would be an aldehyde which could be reacted with a HEMA monomer to produce an acetal linkage.

Another variation of the principle of this invention is the reaction of an active group on an asepticizing agent directly or indirectly with an active group on cellulose acetate-butyrate. For example, parachlorophenyl isocyanate can be reacted with a hydroxyl group on cellulose acetate-butyrate to bond an asepticizing agent to this lens material. This is, of course, but one example of a reactive couple and any other couple may be used.

It is also possible to polymerize the agents possessing the polymerizable group first and then

graft polymerize the monomer mixture onto the polymerized agent. Conversely, the monomer mixture may be polymerized to a low molecular weight prepolymer and then the agent possession a functional group may be polymerized to the prepolymer.

From the foregoing principles and from the examples, which illustrate the invention and are not intended to be all-encompassing (indeed, many thousands of examples would be required to illustrate even all the major applications of the principles of this invention), it will be seen that this invention contemplates contact lenses and contact lens polymers produced from any monomer wherein there is chemically bonded to the polymer, either through polymerization bonding as exemplified by vinyl group polymerization, or chemically bonded to a monomer, prepolymer or polymer (as opposed to solid solutions, etc., for example) regardless of the specific polymers or asepticizing agents involved. Within this broad inventive concept there are many specific discoveries and inventions which are set forth in the preceding specification and which are recognized as inventions within the broad invention just described.

References

1. Rohm and Haas Company, "2-Hydroxyethyl Methacrylate (HEMA) Hydroxypropyl Methacrylate (HPMA)", (CM-43 G/cb).

2. Samour, C.M., "Polymeric Drugs in the Chemotherapy of Microbial Infections", Polymer Preprints, 18(1)559 (Mar., 1977).

3. National Eye Research Foundation Research Report, "Antimicrobial Activity of Contact Lenses Incorporating Disinfectants Through a Process of Polymerization", (Research Project No. JRT-R-C-2, Items 1, 2, 3 and 4); Contacto, 8(3)9 (1964).

4. Wesley, Newton K., "Development and Prophylactic Aspects of the Antimicrobial Lens", Contacto, 9(2)18 (1965).

5. Cepero, Gilberto R., "The Aseptoplast Lens", Contacto, 11(12)11 (1967).

6. Quinones, Enrique G. Lopez, "Studies in Microbiology . . . Including the Use of Bacteriostatic Contact Lenses", Contacto, 11(1)47 (1967).

7. Hill, Richard M., "A Rare 'Taste' for HEMA", International Contact Lens Clinic, 5(5)207-8 (1978).

8. Fichman, S., Baker, V.V., and Horton, H.R., "Iatrogenic Red Eyes in Soft Contact Lens Wearers", International Contact Lens Clinic, 5(5)202 (1978).

9. Bailey, Neal J., "Contact Lens Coating: The Effect on Service Life", Journal of the American Optometric Association, 46(3)214-218 (1975).

10. Newcomer, Paul C., Janoff, Lester E., "Methods of Tinting Soflens® Contact Lenses", American Journal of Optometry & Physiological Optics, 54(3)160-4 (1977).

11. "Tinted Lenses: New 'Life' for Dead Eyes", Contact Lens Forum, 3(3)13-17 (1978).

12. "Heard at the Forum, Tinted Lenses", Contact Lens Forum, 3(8)89 (1978).

13. Dawson, Daniel J., Otteson, Kenneth M., Wang, Patricia C., Wingard, Robert E., Jr., "Soluble Functional Polymers. 2. Utilization of Water-Insoluble Chromophores in Water-Soluble Polymeric Dyes", Macromolecules, 11(2)320-4 (1978).

14. Dawson, Daniel J., Gless, Richard D., Wingard, Robert E., Jr., "Poly(vinylamine Hydrochloride). Synthesis and Utilization for the Preparation of Water-Soluble Polymeric Dyes", J. Am. Chem. Soc., 98, 5996-6000 (1976).

15. Chemical Abstracts, 89:110428r, "Polymer supports in organic synthesis", Pittman, Charles U., Jr., Stahl, G. Allan, Polymer News, 4(6)280-1 (1978).

16. Chemical Abstracts, 89:110434q, "Synthesis and polymerization of unsaturated adamantane derivatives", Novikov, S.S., Khardin, A.P., Radchenko, S.S., Zlotin, S.G., Orlinson, B.S., Izv. Akad. Nauk SSSR, Ser. Khim, (12)2765-7 (1977).

17. Chemical Abstracts, 89:110436s, "Synthesis of pentachlorophenyl esters of unsaturated carboxylic acids", Budzan, B.I., Tolopko, D.K., Yavna, I.M., Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 21(3)452-3 (1978).

18. Chemical Abstracts, 89:75842x, "Water-soluble cationic polymers", Suzuki, Naoyuki, Wada, Yoji, Furuno, Akihisa, Ger. Offen 2,749,295, (18 May 1978).

19. Chemical Abstracts, 89: 75845a, "Contact Lens materials", Japan Kokai 78 35,764, (3 Apr 1978).

20. Chemical Abstracts, 89:216378q, "Colored plastic lenses", Sasaki, Shigeru, Japan Kokai 78 99,279, (30 Aug 1978).

21. Chemical Abstracts, 89:76329x, "Water-soluble polyazo dyes", Arsac, Aime, Frank, Pierre, Fr. Demande 2,349,626 (25 Nov 1977).

22. Chemical Abstracts, 89:112290p, "Synthesis of phthalocyanine reactive dyes with a high degree of binding to cellulosic fibers, Kraska, Jan, Czajkowski, Wojciech, Przegl Wlok, 32(3)128-31 (1978).

23. Chemical Abstracts, 89:112302u, "Water-soluble polymeric yellow dye", Dawson, Daniel J., Otteson, Kenneth M., Davis, Roman, Ger. Offen. 2,754,485, (15 Jun 1978).

24. Chemical Abstracts, 89:112385y, "Water-soluble polymeric dye", Wingard, Robert E., Dawson, Daniel J., Ger. Off. 2,751,262 (24 May 1978).

25. Chemical Abstracts, 89:112395b, "Ultrafiltration purification of a solution of polymeric antraquinone colorants", Cooper, Anthony R., Booth, Robin, G., Matzinger, David P., U.S. Pat. 4,088,572 (9 May 1978).

26. Chemical Abstracts, 89:112396c, "Polymeric anthraquinone dye", Bunes, Leonard A., Ger. Offen. 2,756,003 (29 Jun 1978).

27. Chemical Abstracts, 89:112409j, "Copper phthalocyanine derivatives", Irvine, Alexander McHugh, Blackburn, John Bryce, Ger. Off. 2,753,042 (8 Jun 1978).

28. Chemical Abstracts, 89:112410c, "Copper polychlorophthalocyanines", Fr. Demande 2,357,545 (3 Feb 1978).

29. Chemical Abstracts, 89:112586q, "Polymeric chelate complexes", Brito, Heide, Brito, Victor, Springer, Juergen, Ger. Off. 2,659,242 (29 Jun 1978).

30. Chemical Abstracts, 89:112724h, "Copolymers with biological activity, containing a triorganotin fragment", Bednarski, J.R., Russell, D.B., Belg. 860,051 (15 Feb 1978).

31. Chemical Abstracts, 90:24766p, "Organofunctional siliceous phthalocyanines", Bernal Castillo, J., Kenney, M.E., Rev. Univ.Ind. Santander, Invest., 8(8)5-15 (1978).

32. Chemical Abstracts, 90:24888e, "Antistatic Plastic Lenses", Ikeda, T., Omori, Y., Shudo, S, Ikeda, S., Jpn. Kokai Tokkyo Koho 78 85,874 (28 Jul 1978).

33. Chemical Abstracts, 90:76599f, "Compositions for Correcting Visual Defects", Gaylord, N.G., U.S. 4,120,570, (17 Oct 1978).

34. Davison, John B., Wayne, Kenneth J., "Silicon Phthalocyanine-Siloxane Polymers", Macromolecules, 11(1)186-191 (1978).

35. Conbere, John P., Reed, Firmin P., U.S. 2,824,861, Feb. 25, 1958.

36. Wichterle, Otto, Lim, Drahoslav, U.S. 2,976,576, Mar. 28, 1961.

37. Ham, George E., U.S. 3,072,622, Jan. 8, 1963.

38. Lang, John L., Jones, Clifford, Roche, Arthur F., U.S. 3,080,348, Mar. 5, 1963.

39. Jefferson, Donald E., U.S. 3,172,868, Mar. 9, 1965.

40. Gusewitch, Lorraine, Chevalier, Ruth M., U.S. 3,189,914, June 15, 1965.

41. Wichterle, Otto, Lim, Drahoslav, U.S. 3,220,960, Nov. 30, 1965.

42. Glavis, Frank J., Hamori, Eugene A., U.S. 3,245,932, Apr. 12, 1966.

43. Suen, Tzeng Jiueq, Meisenhelder, William C., U.S. 3,284,394, Nov. 8, 1966.

44. Brudney, Harry, U.S. 3,286,394, Nov. 22, 1966.

45. Wichterle, O., U.S. 3,361,858, Jan. 2, 1968.

46. Wichterle, O., U.S. 3,408,429, Oct. 28, 1969.

47. Siegel, R., U.S. 3,454,332, July 8, 1969.

48. Creighton, C.P., U.S. 3,489,491, Jan. 13, 1970.

49. Wichterle, Otto, U.S. 3,496,254, Feb. 17, 1970.

50. Wichterle, O., U.S. 3,499,862, Mar. 10, 1970.

51. Wichterle, O., U.S. 3,542,907, Nov. 24, 1970.

52. Seiderman, M., U.S. 3,503,942, Mar. 31, 1970.

53. Spivack, M., U.S. 3,536,386, Oct., 1970.

54. Wichterle, O., U.S. 3,557,261, Jan. 19, 1971.

55. Zeltzer, Harry I., U.S. 3,586,423, June 22, 1971.

56. Seiderman, Maurice, U.S. 3,639,524, Feb. 1, 1972.

57. Eweil, David G., U.S. 3,647,736, Mar. 7, 1972.

58. Wichterle, O., U.S. 3,679,504, July 25, 1972.

59. Wichterle, O., U.S. 3,699,089, Oct. 17, 1972.

60. LeGrand, Joseph A., Fuhrman, Art, U.S. 3,712,718, Jan. 23, 1973.

61. Zeltzer, Harry I., U.S. 3,701,590, Oct. 31, 1972.

62. Gustafson, Robert, U.S. 3,728,315, Apr. 17, 1973.

63. Stamberger, Paul, U.S. 3,758,448, Sept. 11, 1973.

64. Wichterle, O., Krejei, Lubornir, U.S. 3,767,759, Oct. 23, 1973.

65. Kliment, Karel, Rutherford, John M., Jr., U.S. 3,784,540, Jan. 8, 1974.

66. Labana, Santokh S., Chang, Yun Feng, U.S. 3,787,340, Jan. 22, 1974.

67. Wichterle, Otto, U.S. 3,822,089, July 2, 1974.

68. Gustafson, Robert, U.S. 3,892,721, July 1, 1975.

69. Holcombe, Frank O., Jr., U.S. 3,926,892, Dec. 16, 1975.

70. Barkdoll, Archie E., U.S. 3,940,207, Feb. 24, 1976.

71. Barkdoll, Archie E., England, David C., U.S. 3,944,347, Mar. 16, 1976.

72. Stamberger, Paul, U.S. 3,947,401, Mar. 30, 1976.

73. Cleaver, Charles S., U.S. 3,950,315, Apr. 13, 1976.

74. Leeds, Harry R., U.S. 3,951,528, Apr. 20, 1976.

75. Mancini, William L., Korb, Donald R., Refojo, Miguel F., U.S. 3,957,362, May 18, 1976.

76. Fujiwara, Hiroshi, Sekiya, Masaaki, Suzuki, Hiroshi, U.S. 3,963,662, June 15, 1976.

77. Miller, John J., Baus, Richard E., U.S. 3,970,633, July 20, 1976.

78. Dyckman, E.J., et al, U.S. 3,979,354, Sept. 7, 1976.

79. Kaetsu, Isao, Kumakura, Minoru, Ito, Akihiko, Maeda, Yuji, U.S. 3,983,083, Sept. 28, 1976.

80. Masuhara, Eiichi, Tarumi, Niro, Tsuchiya, Makoto, U.S. 3,988,274, Oct. 26, 1976.

81. Shepherd et al, U.S. 3,990,381, November 9, 1976.

82. Steckler, Robert, Linder, Seymour Martin, U.S. 4,009,201, Feb. 22, 1977.

83. Temple, Stanley, U.S. 4,013,627, Mar. 22, 1977.

84. Loshaek, Samuel, U.S. 4,028,295, June 7, 1977.

85. Wang, Patricia C., Wingard, Robert E., U.S. 4,051,138, Sept. 27, 1977.

86. Cooper, Anthony R., Booth, Robin G., Matzinger, David P., U.S. 4,088,572, May 9, 1978.

87. Erickson, Charles E., U.S. 4,093,361, June 6, 1978.

88. Sieglaff, Charles L., Hora, Charles J., Tiefenbach, Joseph P., U.S. 4,097,657, June 27, 1978.

89. Merrill, Edward W., U.S. 4,099,859, July 11, 1978.

90. Vrancker, M., Smets, G., J. Polymer Sci., 14, 521 (1954).

91. Chemical Abstracts, 89:112482c, Stahl, G.A., Pitman, C.V., Jr., J. Coating Technology, 50:625,639 (1978).

92. Chemical Abstracts, 90:72265w, Sadurski, E. Alan; Ilsley, William H.; Thomas, Ruthanne D.; Glick, Milton D.; Oliver, John P., J. Am. Chem. Soc., 1978, 100(24), 7761-2.

93. Chemical Abstracts, 90:72534h, Katz, D.; Zewi, I.G., J. Polym. Sci., Polym. Chem. Ed., 1978, 16(3), 597-614.

94. Chemical Abstracts, 90:72865s, Johnson, Edward F.; Carlsen, John S., U.S. 4,117,027.

95. Chemical Abstracts, 90:73134q, Yokokawa, Kiyoshi; Shimamoto, Noboru; Takeuchi, Kinya, Jpn. Kokai Tokkyo Koho 78,117,051.

96. Chemical Abstracts, 90:76599f, Gaylord, Norman G., U.S. 4,120,570.

97. Chemical Abstracts, 90:43848h, Harris, James E.; Parish, Ben D., U.S. 4,116,549.

98. Chemical Abstracts, 90:142190u, Mueller, Karl F.; Kleiner, Eduard K., U.S. 4,136,250.

99. Chemical Abstracts, 90:121703y, Brady, William T.; Saidi, Kazem, J. Org. Chem., 1979, 44(5), 733-7.

100. Chemical Abstracts, 90:122239p, Wynne, Kenneth J.; Davidson, John, U.S. Pat. Appl. 880,515.

101. Chemical Abstracts, 90:122252n, Wynne, Kenneth J.; Davidson, John, U.S. Pat. Appl. 880,514.

102. Chemical Abstracts, 90:122593z, Takamizawa, Minoru; Inoue, Yoshio; Inosaka, Toshifumi; Abe, Kaname; Takano, Koichi, Jpn. Kokai Tokkyo Koho 78,139,653.

103. Chemical Abstracts, 90:20326x, Brodrick, John D., Arch. Ophthalmol. (Chicago), 1978, 96(11), 2021-6.

104. Chemical Abstracts, 90:22201b, Spielvogel, David E.; Frye, Cecil L., J. Organomet. Chem., 1978, 161(2), 165-9.

105. Chemical Abstracts, 90:24170q, Falcetta, Joseph James; Frienos, Gary Dean; Niu, Gregory Chen-Chie, Fr. Demande 2,365,606.

106. Chemical Abstracts, 90:24766p, Bernal Castillo, Jaime; Kenney, Malcolm E., Rev. Univ. Ind. Santander, Invest., 1978, 8(8), 5-15.

107. Chemical Abstracts, 90:24888e, Ikeda, Tadayoshi; Omori, Yasushi; Shudo, Shinji; Ikeda, Saizo, Jpn. Kokai Tokkyo Koho 78 85,874.

108. Chemical Abstracts, 90:28926p, Schmickl, Hans, DOZ. Dtsch. Optikerztg., 1978, 33(2), 99-101, 103-4.

109. Chemical Abstracts, 90:28984f, Fanti, Peter, DOZ. Dtsch. Optikerztg., 1978, 33(6), 75-7.

110. Chemical Abstracts, 90:29040g, Wajs, Georges, Ger. Offen. 2,813,558.

111. Chemical Abstracts, 90:29511m, Komarova, A.B.; Dubyaga, E.G.; Tarakanov, O.G., Kolloidn. Zh., 1978, 40(5), 997-9.

I CLAIM AS MY INVENTION:

1. A contact lens comprising:

(a) a lens polymer;

(b) an asepticizing agent chemically bonded to said lens polymer such that the agent will not leach out of the lens polymer.

2. The contact lens of Claim 1 wherein the polymer is a hydrogel.

3. The contact lens of Claim 1 wherein the asepticizing agent is chemically bonded through carbon-carbon double bond polymerization reaction with lens monomer or lens prepolymer.

4. A method of fabricating an aseptic contact lens polymer comprising:

(a) mixing an asepticizing agent having a polymerizable group with a lens monomer or prepolymer system which is polymerizable with the polymerizable group on the asepticizing agent, and

(b) co-polymerizing said asepticizing agent with said lens monomer to form a chemically bonded asepticized lens polymer.

5. A method of fabricating an aseptic contact lens polymer comprising:

(a) polymerizing asepticizing agent having a polymerizable functional group; and

(b) polymerizing lens monomer onto said polymerizable asepticizing agent.

6. A method of fabricating an aseptic contact lens polymer comprising:

(a) polymerizing a lens polymer or prepolymer having polymerizable active groups on the lens polymer or prepolymer; and

(b) condensation polymerizing a condensation polymerizable asepticizing agent onto the polymer or prepolymer to form a lens polymer or prepolymer having chemically bonded thereto biologically active asepticizing groups.

7. A method of fabricating an aseptic contact lens polymer comprising:

(a) polymerizing a lens polymer or prepolymer having addition polymerizable active groups on the lens polymer or prepolymer; and

(b) addition polymerizing a polymerizable group containing asepticizing agent onto the polymer or prepolymer to form a lens polymer or prepolymer having chemically bonded thereto biologically active asepticizing groups.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US80/00698

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL.[3] C08F/20/10
U.S. CL. 525/328

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
US	525/328

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X	U.S., A 3872128 PUBLISHED 18 MARCH 1975 BYCK	1-7
X	U.S., A 3927206 PUBLISHED 16 DECEMBER 1975 BLANK ET. AL.	1-7
A	U.S., A 4006147 PUBLISHED 01 FEBRUARY 1977 HRABAK ET. AL.	

* Special categories of cited documents: [15]

"A" document defining the general state of the art

"E" earlier document but published on or after the international filing date

"L" document cited for special reason other than those referred to in the other categories

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but on or after the priority date claimed

"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention

"X" document of particular relevance

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
25 AUGUST 1980	01 OCT 1980
International Searching Authority [1]	**Signature of Authorized Officer** [20]
ISA/US	Harry Wong Jr. HARRY WONG, JR.